Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1-157. (canceled)

158. (Currently Amended) A method for identifying a protein target as being able to bind a ligand, comprising:

(a) providing a molecule comprising a methotrexate moiety ~~which binds to dihydrofolate reductase,~~ covalently ~~bonded~~ linked to the ligand, which methotrexate moiety binds to a dihydrofolate reductase;

(b) introducing the molecule into a cell which i) expresses a first fusion protein comprising ~~a~~ the dihydrofolate reductase capable of binding the methotrexate moiety, ii) expresses a second fusion protein comprising the protein target, wherein ~~one of~~ either the first ~~and~~ or second fusion protein ~~proteins~~ also comprises a transcription activator domain and the other fusion protein comprises a DNA-binding domain, and iii) has a reporter gene, wherein expression of the reporter gene is conditioned on the proximity of the first fusion protein to the second fusion protein and wherein the DNA-binding domain binds upstream of the reporter gene;

(c) permitting the molecule to bind to the first fusion protein and to the second fusion protein so as to activate the expression of the reporter gene; and

(d) selecting the cell if it expresses the reporter gene,

so as to thereby identify the protein target as being able to bind the ligand.

159. (Currently Amended) The method of claim 158, wherein the protein target is encoded by ~~a DNA from the group consisting of~~ genomic DNA[[,]] or a cDNA ~~and synthetic DNA~~.

160. (Previously Presented) The method of claim 158, wherein the ligand has a known biological function.

161. (Previously Presented) The method of claim 158, wherein the first fusion protein is (dihdrofolate reductase)-(DNA-binding domain).

162. (Previously Presented) The method of claim 158, wherein the first fusion protein is (dihdrofolate reductase)-(LexA).

163. (Previously Presented) The method of claim 158, wherein the first fusion protein is (dihdrofolate reductase)-(transcription activation domain).

164. (Previously Presented) The method of claim 158, wherein the first fusion protein is (dihdrofolate reductase)-(B42).

165. (Previously Presented) The method of claim 158, wherein the second fusion comprises a DNA-binding domain.

166. (Previously Presented) The method of claim 158, wherein the second fusion protein comprises LexA.

167. (Previously Presented) The method of claim 158, wherein the second fusion protein comprises a transcription activation domain.

168. (Previously Presented) The method of claim 158, wherein the second fusion protein comprises B42.

169. (Currently Amended) The method of claim 158, wherein the cell is ~~*S. cerevisiae* or *E. coli*~~ *S. cerevisiae* or *E. coli*.

170. (Previously Presented) The method of claim 158, wherein the reporter gene is lacZ, Gal4 or Ura-3.

171. (Previously Presented) The method of claim 158, wherein the cell is a bacterial cell, the molecule comprises a methotrexate moiety bound to the ligand, the first fusion protein comprises a dihydrofolate reductase and a LexA, the second fusion protein comprises the protein target and B42, and the reporter gene is LacZ.

172. (Previously Presented) The method of claim 158, wherein the cell is a yeast cell, the molecule comprises a methotrexate moiety bound to the ligand, the first fusion protein comprises a dihydrofolate reductase and a LexA,

the second fusion protein comprises the protein target and B42, and the reporter gene is Gal4.

173-176. (Cancelled)

177. (Withdrawn - Currently Amended) In a method for determining if a protein interacts with a ligand in vivo, wherein the method comprises activating a reporter gene by contacting a cell expressing two fusion proteins, the first comprising a dihydrofolate reductase ~~ligand binding~~ domain fused to a DNA-binding domain, which DNA-binding domain binds upstream of the reporter gene, and the second comprising a transcription activation domain fused to the protein, with a covalently linked hybrid-ligand so as to activate the reporter gene, the improvement comprising a covalently linked hybrid-ligand having a methotrexate moiety, which methotrexate moiety binds to the dihydrofolate reductase.

178. (Withdrawn) The method of claim 177, wherein the DNA-binding domain is a LexA DNA-binding domain.

179. (Withdrawn) The method of claim 177, wherein the transcription activation domain is B42.

180. (Withdrawn) The method of claim 177, wherein the reporter gene is LacZ or Gal4.